

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. With this amendment, claims 26 has been amended, no claims have been cancelled, and no claims have been added. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. Thus, claims 26, and 29-38 are pending in the application.

Claim Rejections - 35 USC § 112: New Matter

Claims 26 and 29-35 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges that “a hot spot having a three dimensional porous structure, the hot spot being stationary within the second channel and comprising a plurality of cross-linked nanoparticles aggregates affixed within the hot spot within the second channel, wherein the hot spot enhances a Raman signal of the single nucleotide” is new matter. Applicants respectfully traverse the rejection.

If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751, (CCPA 1972)(stating “the description need not be in *ipsis verbis* [i.e., “in the same words”] to be sufficient”). (See also MPEP 2163(II)(3)(a)). In the office action, the Examiner states “The limitation suggests that a hot spot is a separate entity of the apparatus and is separate from the cross-linked nanoparticles aggregates. However, ... The teachings of the specification hence suggest that the cross-linking of the nanoparticles aggregates form hot spots and thus hot spots do not form nanoparticle aggregates.” (Office action, p.3, l.6 to p.4, l.2). The Examiner also states “Likewise, there is no teachings anywhere in the specification which would suggest that the nanoparticles

which form “hot spots” to be porous or three-dimensional. In fact the nanoparticles are metal compounds which are not porous.” (Id. at p.5, l.5-7).

Applicant believes that previously presented claim 26 has caused confusion. In response, Applicant has amended claim 26 to clarify that the aggregate of nanoparticles is porous, not the individual nanoparticles. Support for this feature can be found in paragraph [0025] of the published application and Fig. 1. Further, as discussed in paragraphs [0037] and [0102], the entire aggregate of cross-linked nanoparticles forms the “hot spot.” Applicant submits that one of ordinary skill in the art reading the specification would understand that the Applicants were in possession of an apparatus having “a three-dimensional porous structure comprising a plurality of cross-linked nanoparticle aggregates affixed within the second channel, the three-dimensional porous structure comprising a hot spot that enhances a Raman signal of the single nucleotide” as recited in amended claim 26. Applicants therefore respectfully request withdrawal of the rejection.

Claim Rejections - 35 USC § 112

Claims 26 and 29-38 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states “it is unclear how the ‘hot spot’ modifies the structure of the apparatus. A hot spot would not be readily apparent in the apparatus until the apparatus has function in a manner to display a Raman signal, which would be enhanced or brighter based on the presence of hot spots.” (Office action, p.5, l.5). Applicants respectfully traverse the rejection.

As discussed above, independent claim 26 was amendment to clarify that the apparatus has “a three-dimensional porous structure comprising a plurality of cross-linked nanoparticle aggregates affixed within the second channel, the three-dimensional porous structure comprising a hot spot that enhances a Raman signal of the single nucleotide.” Applicant agrees that the hot spot would not be apparent until the apparatus was in use. The present amendment clarifies that the

structure responsible for the hot spot is the aggregate of cross-linked nanoparticles that are affixed in the second channel. Applicant submits that amended claim 26 is definite and respectfully requests withdrawal of the rejection.

Claim Rejections - 35 USC § 103

Claims 26, 29-34 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash (citation made of record in prior Office action in view of Shipway (citation made of record) and further in view of Nie et al (Science, vol. 275, pages 1102-1106, 1997). Claims 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash in view of Shipway and Nie et al as previously applied above in view of Ulmer et al (5674743) and further in view of Vo-Dihn (5306403). Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shipwash in view of Shipway and Nie et al as previously applied above in view of Williams et al (citation made of record in prior Office action). Applicants respectfully traverse the rejections.

On pages 5 and 6 of the office action, the Examiner notes that only the structural features of an apparatus claim distinguish the claim from the prior art, not the intended use. Applicants agree. Applicants, note and appreciate, however, that the method claims of the corresponding applications were examined and allowed by the present Examiner. Applicants further note that amended claim 26 is the apparatus that corresponds to the allowed methods. Prior to the claimed invention, there was no apparatus that was capable of detecting a *single* nucleotide by Raman. Therefore, it is not just the methods of the claims that are patentable but also the pending apparatus claims should be patentable.

Further, in support of the rejections, the Examiner states “the structure of the hot spot being a three-dimensional porous structure is inherent in the teachings of nanoparticle aggregates as taught by Shipway and Nie et al.” (Office action, p.7, l.16-18). Shipway, however, merely discloses nanoparticle arrays on surfaces. Shipway et al. do not teach an apparatus capable of detecting single nucleotides. Further, Nie merely mentions the existence of nanoparticle aggregates.

As noted by the Examiner, Nie teaches that the observed hot spots are due to single hot particles or a single hot particle trapped in an aggregate. Nie does not teach or suggest a hot spot comprising an aggregate of cross-linked nanoparticles.

Additionally, "when an applicant demonstrates substantially improved results [] and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary." In re Soni, 54 F.3d 746, 751 (Fed. Cir. 1995). As evidenced in Table I and paragraph [0103] of the specification ([0125] of printed pub.), the present invention is capable of detecting single nucleotides. The Examiner argues that the "claims also do not depict the unexpected results asserted by Applicant as the art recognizes the usefulness and predictability of Raman spectroscopy for detecting single molecules and for sequencing DNA molecules in an efficient manner." (Office action, p. 15, 1.18-20). While, the prior art may have recognized the usefulness of detecting single molecules, Applicants were the first to do so.

Additionally, the Examiner's states that the "MPEP states that 'objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.'" Applicants notes, however, the MPEP citation only applies to situations in which evidence is not in the original specification. In reversing the Board's finding of obviousness, the Federal Circuit noted:

Soni's specification contains more than mere argument or conclusory statements; it contains specific data indicating improved properties. It also states that the improved properties provided by the claimed compositions "are much greater than would have been predicted given the difference in their molecular weights." 54 F.3d at 750.

Applicants, as did the applicant in Soni, have provided evidence of unexpected results in the specification. It is undisputed that Applicants invented the first apparatus capable of detecting a

single nucleotide with Raman. Applicants therefore respectfully request withdrawal of the rejections.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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